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NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
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NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available

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=> s tnf? or (tumor necrosis factor)
L1      247879 TNF? OR (TUMOR NECROSIS FACTOR)

=> s antisense? or ribozyme?
L2       85540 ANTISENSE? OR RIBOZYME?

=> s l1 and l2
L3        2126 L1 AND L2

=> s l3 and inhibit?
L4        1399 L3 AND INHIBIT?

=> s l4 and inflamm?
L5         308 L4 AND INFLAMM?

=> s l5 and inhibit? (5n) antisense
L6         124 L5 AND INHIBIT? (5N) ANTISENSE

=> s l6 and (prevent or reduc? or inhibit?) (5n) inflam?
L7          20 L6 AND (PREVENT OR REDUC? OR INHIBIT?) (5N) INFLAM?

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L8           16 DUP REMOVE L7 (4 DUPLICATES REMOVED)

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     (FILE 'HOME' ENTERED AT 17:34:47 ON 01 MAY 2002)

     FILE 'BIOSIS, MEDLINE, SCISEARCH, CA' ENTERED AT 17:34:56 ON 01 MAY 2002
L1      247879 S TNF? OR (TUMOR NECROSIS FACTOR)
L2       85540 S ANTISENSE? OR RIBOZYME?
L3        2126 S L1 AND L2
L4        1399 S L3 AND INHIBIT?
L5         308 S L4 AND INFLAMM?
L6         124 S L5 AND INHIBIT? (5N) ANTISENSE
L7          20 S L6 AND (PREVENT OR REDUC? OR INHIBIT?) (5N) INFLAM?
L8          16 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1-16 bib abs
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L8 ANSWER 1 OF 16 CA COPYRIGHT 2002 ACS
AN 135:236419 CA
TI **Inhibition** of protein kinase Tpl2 to treat **inflammatory** diseases
IN Tsichlis, Philip N.
PA Thomas Jefferson University, USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001066559	A1	20010913	WO 2001-US7588	20010308

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI US 2000-522775 A 20000308

AB The present invention is directed to animal having functionally disrupted endogenous Tpl2. These animals are resistant to Lps induced endotoxin shock and **TNF**.alpha. - mentioned **inflammatory** disease. A method of identifying Tpl2 specific **inhibitors** of endotoxin shock or antagonists to **inflammation** on and a method of treating or preventing **TNF**.alpha. - mediated **inflammatory** diseases and Lps induced endotoxin shock in animals are also within the scope of this invention. The present invention also provides protein and cDNA sequences of human and rat protein kinase Tpl2 gene.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 16 CA COPYRIGHT 2002 ACS
AN 134:261249 CA
TI TRAIL: an **inhibitor** of autoimmune **inflammation** and cell cycle progression
IN Chen, Youhai
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001022987	A1	20010405	WO 2000-US26862	20000929

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-157222P P 19990930

AB The invention provides a method for achieving normal levels of cellular apoptosis in non-transformed cells of a patient by administering to the patient a therapeutically effective amt. of purified TRAIL ligand or active fragment thereof. In particular, a method is provided to a patient suffering from an autoimmune disease or condition, e.g. arthritis, encephalomyelitis or multiple sclerosis or autoimmune **inflammation** in the CNS. The invention further provides a method of blocking the activity of an endogenous TRAIL receptor or **inhibitor** in a patient by administering to the patient a therapeutically effective amt.

of a purified TRAIL agonist, in an amt. sufficient to enhance the patient's level of TRAIL ligand. In particular, such method is provided to enhance ameliorate or restore cellular apoptosis in non-transformed cells of the patient.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 16 CA COPYRIGHT 2002 ACS
AN 134:141771 CA
TI Methods using PPAR.delta. **inhibitors** for treatment of vascular diseases, cancer, Alzheimer's disease, and **inflammatory** disorders, and drug screening methods
IN Palmer, Colin Neil Alexander; Vosper, Helen; Wolf, Charles Roland
PA The University of Dundee, UK
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001007066	A2	20010201	WO 2000-EP6986	20000719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1999-17405 A 19990723
AB A method of preventing or reducing foam cell development from macrophages, or removing foam cells, in a patient comprises administering an effective amt. of an **inhibitor** of PPAR.delta. activity. A method of preventing or treating a vascular disease assocd. with plaque formation and/or thrombotic blockage of the blood vessels in a patient comprises administering to the patient an effective amt. of an **inhibitor** of PPAR.delta. activity. Also disclosed are methods for the treatment of cancer, Alzheimer's disease, and **inflammatory** disorders.

L8 ANSWER 4 OF 16 CA COPYRIGHT 2002 ACS
AN 133:27867 CA
TI Novel **inhibitor** of nuclear factor-.kappa.B, RelA-associated **inhibitor**, recombinant expression, and use in disease diagnosis
IN Okamoto, Takashi
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000032628	A1	20000608	WO 1999-JP6753	19991202

W: KR, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

JP 2000224993	A2	20000815	JP 1999-342773	19991202
EP 1146054	A1	20011017	EP 1999-973038	19991202

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI JP 1998-344038 A 19981203

WO 1999-JP6753 W 19991202

AB A human RelA-assocd. **inhibitor** (RAI); a cDNA encoding it; **antisense** oligonucleotide; a cloning or expression vector; host cells; an antibody against the polypeptide; pharmaceutical compns. contg. the peptide or the antibody; and a method for diagnosing a disease by using the antibody against RAI, are claimed. The identification and characterization of a novel protein, RelA-assocd. **inhibitor** (RAI), that binds to the NF-.kappa.B subunit p65 (RelA) and **inhibits** its transcriptional activity is reported. RAI gene was isolated in a yeast two-hybrid screen using the central region of p65 as bait. The phys. interaction was confirmed in vitro using recombinant proteins as well as in vivo by immunopptn./Western blot assay. RAI gene encodes a protein with homol. to the C-terminal region of 53BP2 contg. four consecutive ankyrin repeats and an Src homol. 3 domain. RAI mRNA was preferentially expressed in human heart, placenta, and prostate. Despite its similarity to 53BP2, RAI did not interact with p53 in a yeast two-hybrid assay. RAI **inhibited** the action of NF-.kappa.B p65 but not that of p53 in transient luciferase gene expression assays. Similarly, RAI **inhibited** the endogenous NF-.kappa.B activity induced by **tumor necrosis factor**-.alpha.. RAI specifically **inhibited** the DNA binding activity of p65 when co-transfected in 293 cells. RAI protein appeared to be located in the nucleus and colocalized with NF-.kappa.B p65 that was activated by **TNF**-.alpha.. These observations indicate that RAI is another **inhibitor** of NF-.kappa.B in addn. to I.kappa.B proteins and may confer an alternative mechanism of regulation.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 16 CA COPYRIGHT 2002 ACS

AN 132:343312 CA

TI **Inhibition** of the formation of vascular hyperpermeability using **inhibitors** of KDR tyrosine kinase

IN Arnold, Lee D.; Bousquet, Peter F.

PA BASF Aktiengesellschaft, Germany

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000027414	A2	20000518	WO 1999-US25903	19991103
	WO 2000027414	A3	20000908		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9915139	A	20010807	BR 1999-15139	19991103
	EP 1126842	A2	20010829	EP 1999-962685	19991103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002218	A	20010618	NO 2001-2218	20010504
PRAI	US 1998-107462P	P	19981106		
	WO 1999-US25903	W	19991103		

AB Vascular hyperpermeability in individuals is a prelude to a no. of physiol. events that are often deleterious. Among these events is the formation of edema, diapedesis, aberrant trans-endothelial exchange,

extravasation, exudation and effusion, matrix deposition (often with abnormal stromal proliferation) and vascular hypotension. Vascular hyperpermeability and the subsequent events can be **inhibited** by the administration of a compd. that **inhibits** the enzyme activity of the VEGF tyrosine kinase receptor known as KDR tyrosine kinase. Preferred administered compds. selectively **inhibit** the function of KDR tyrosine kinase but do not block the activity of Flt-1 tyrosine kinase which is another VEGF tyrosine kinase receptor.

L8 ANSWER 6 OF 16 CA COPYRIGHT 2002 ACS
AN 133:72841 CA
TI The **inhibition** of apoptosis in myositis and in normal muscle cells
AU Nagaraju, Kanneboyina; Casciola-Rosen, Livia; Rosen, Antony; Thompson, Cynthia; Loeffler, Lisa; Parker, Tomasina; Danning, Carol; Rochon, Paul J.; Gillespie, John; Plotz, Paul
CS Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SO Journal of Immunology (2000), 164(10), 5459-5465
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB The mechanism of injury and death of muscle cells in the **inflammatory** myopathies (dermatomyositis, polymyositis, and inclusion body myositis) remains obscure. We and others have not detected apoptosis in the muscle biopsies from patients with myositis despite clear evidence of cell damage and loss. We provide evidence in this study that Fas ligand (FasL) as well as Fas is present on muscle cells and **inflammatory** cells in myositis biopsies; Fas is present on most muscle cells and lymphocytes, and FasL is present on degenerating muscle cells and many infiltrating mononuclear cells. The expression of both Fas and FasL in the inflamed tissue makes the absence of apoptosis more striking. To address the mechanisms of this resistance to classical apoptosis in muscle cells, we have investigated the expression of the antiapoptotic mol. FLICE (Fas-assocd. death domain-like IL-1-converting enzyme)-**inhibitory** protein (FLIP) in muscle biopsies of myositis patients and in cultured human skeletal muscle cells. Using laser capture microscopy, we have shown that FLIP is expressed in the muscle fibers and on infiltrating lymphocytes of myositis biopsies. Furthermore, we have shown that FLIP, but not Bcl-2, is expressed in cultured human skeletal muscle cells stimulated with proinflammatory cytokines, and **inhibition** of FLIP with **antisense** oligonucleotides promotes significant cleavage of poly-(ADP-ribose) polymerase autoantigen, a sensitive indicator of apoptosis. These studies strongly suggest that the resistance of muscle to Fas-mediated apoptosis is due to the expression of FLIP in muscle cells in the **inflammatory** environment in myositis.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2000:218431 BIOSIS
DN PREV200000218431
TI Transforming growth factor-beta **inhibits** lipopolysaccharide-stimulated expression of **inflammatory** cytokines in mouse macrophages through downregulation of activation protein 1 and CD14 receptor expression.
AU Imai, Kenichi; Takeshita, Akira; Hanazawa, Shigemasa (1)
CS (1) Department of Oral Microbiology, Meikai University School of Dentistry, Keyakidai, Sakado City, Saitama, 350-0283 Japan

SO Infection and Immunity, (May, 2000) Vol. 68, No. 5, pp. 2418-2423.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB The septic shock that occurs in gram-negative infections is caused by a cascade of **inflammatory** cytokines. Several studies showed that transforming growth factor-beta1 (TGF-beta1) **inhibits** this septic shock through suppression of expression of the lipopolysaccharide (LPS)-induced **inflammatory** cytokines. In this study, we investigated whether TGF-beta1 **inhibition** of LPS-induced expression of **inflammatory** cytokines in the septic shock results from downregulation of LPS-stimulated expression of CD14, an LPS receptor. TGF-beta1 markedly **inhibited** LPS stimulation of CD14 mRNA and protein levels in mouse macrophages. LPS-stimulated expression of CD14 was dramatically **inhibited** by addition of **antisense**, but not sense, c-fos and c-jun oligonucleotides. Since TGF-beta1 pretreatment **inhibited** LPS-stimulated expression of c-fos and c-jun genes and also the binding of nuclear proteins to the consensus sequence of the binding site for activation protein 1 (AP-1), a heterodimer of c-Fos and c-Jun, in the cells, TGF-beta1 **inhibition** of CD14 expression may be a consequence of downregulation of AP-1. LPS-stimulated expression of interleukin-1beta and **tumor necrosis factor** alpha genes in the cells was **inhibited** by addition of CD14 **antisense** oligonucleotide. Also, TGF-beta1 **inhibited** the LPS-stimulated production of both **inflammatory** cytokines by the macrophages. In addition, TGF-beta1 **inhibited** expression of the two cytokines in several organs of mice receiving LPS. Thus, our results suggest that TGF-beta1 **inhibition** of LPS-stimulated **inflammatory** responses resulted from downregulation of CD14 and also may be a possible mechanism of TGF-beta1 **inhibition** of LPS-induced septic shock.

L8 ANSWER 8 OF 16 MEDLINE
AN 2000209759 MEDLINE
DN 20209759 PubMed ID: 10745672
TI [Chronic **inflammatory** bowel disease--pathogenic concepts and therapeutic perspectives].
Kronisk **inflammatorisk** tarmsygdom--patogenetiske overvejelser og terapeutiske perspektiver.
AU Madsen J R
CS Medicinsk Gastroenterologisk Afdeling C, Amtssygehuset i Herlev.
SO UGESKRIFT FOR LAEGER, (2000 Mar 6) 162 (10) 1361-6. Ref: 25
Journal code: WM8; 0141730. ISSN: 0041-5782.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Danish
FS Priority Journals
EM 200004
ED Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000420
AB Chronic **inflammatory** bowel disease (IBD) is considered to be a consequence of inappropriate upregulation of immune reactions evoked by the colonic microflora. Abnormalities observed in IBD may be explained, at least in part, by an unfavourable balance between pro- and anti-**inflammatory** cytokines. Conventional drug treatment of IBD may soon be replaced by more selective **inhibitors** that act centrally in the **inflammatory** process. Immunoneutralisation with chimeric anti-tumour necrosis factor-alpha (**TNF** alpha) antibodies reduces treatment refractory IBD, including fistular Chrons' disease, but

recombinant human **TNF** alpha-receptor fusion proteins may be equally effective with potentially fewer side effects. This view also applies to chimeric antibodies directed against cytokines or adhesion molecules. Potentially more promising are **antisense** oligonucleotides and matrix-metalloproteinase **inhibitors**. Whether sustained remission can be achieved probably depends on successful unravelling of the aetiology of IBD.

L8 ANSWER 9 OF 16 CA COPYRIGHT 2002 ACS
AN 128:229331 CA
TI Use of phosphorothioate-modified oligodeoxynucleotides to **inhibit** NF-.kappa.B expression and lymphocyte function
AU Khaled, Annette R.; Butfiloski, Edward J.; Sobel, Eric S.; Schiffenbauer, Joel
CS Department of Molecular Genetics and Microbiology, Division of Rheumatology and Clinical Immunology, University of Florida, Gainesville, FL, 32610, USA
SO Clin. Immunol. Immunopathol. (1998), 86(2), 170-179
CODEN: CLIIAT; ISSN: 0090-1229
PB Academic Press
DT Journal
LA English
AB NF-.kappa.B is a potential target for immunosuppressive therapy. Two methods were evaluated to **inhibit** NF-.kappa.B: the **antisense** (AS) approach in which single-stranded oligodeoxynucleotides (ODNs) bind the mRNA for the RelA subunit of NF-.kappa.B and the transcription factor decoy (TFD) approach in which double-stranded ODNs bind the NF-.kappa.B protein. AS and TFD **inhibited** NF-.kappa.B binding and decreased total IgG and anti-dsDNA antibody prodn. in splenocytes from the BXSB/Yaa autoimmune mouse strain. **TNF**-.alpha. expression was reduced by AS and TFD, as were the levels of IL-2. But AS effects did not last beyond 24 h, whereas TFD **inhibited** cytokine prodn. after 72 h. AS had no effect upon IL-6, while the TFD reduced the secretion of IL-6. Therefore, the suppression of immune response mediators by AS or TFD, through **inhibition** of NF-.kappa.B, is substantial. These **inhibitors** can serve as novel choices for therapy in the treatment of autoimmune disorders.

L8 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1997:405741 BIOSIS
DN PREV199799711944
TI **Antisense** strategies for **inhibition** of **tumor necrosis factor**-alpha synthesis.
AU Hartmann, Gunther; Krug, Anne; Bidlingmaier, Martin; Eigler, Andreas; Endres, Stefan (1)
CS (1) Medizinische Klin., Klinikum Innenstadt, Ludwig-Maximilians-Univ., Munich Germany
SO Nucleosides & Nucleotides, (1997) Vol. 16, No. 5-6, pp. 629-634.
ISSN: 0732-8311.
DT Article
LA English
AB The proinflammatory cytokine **tumor necrosis factor**-alpha (**TNF**) plays a key role in **inflammatory** disease. **Antisense** oligonucleotide-mediated **inhibition** of monocyte-derived **TNF** synthesis may provide a valuable tool for therapeutic intervention. We established a model allowing specific suppression of **TNF** synthesis by oligonucleotides.

L8 ANSWER 11 OF 16 CA COPYRIGHT 2002 ACS
AN 125:158040 CA

TI In vitro efficacy of morpholino-modified **antisense** oligomers directed against **tumor necrosis factor** -.alpha. mRNA

AU Taylor, Margaret Flynn; Paulauskis, Joseph D.; Weller, Dwight D.; Kobzik, Lester

CS Physiol. Program, Harvard Sch. Public Health, Boston, MA, 02115, USA

SO J. Biol. Chem. (1996), 271(29), 17445-17452
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB Chem. modification of **antisense** oligonucleotides to increase nuclease resistance may improve their efficacy within enzyme-rich cellular targets (e.g. macrophages). We evaluated a panel of morpholino **antisense** oligomers (M-AS) for their ability to **inhibit** macrophage **tumor necrosis factor**-.alpha. (**TNF**-.alpha.) release and compared them to phosphodiester (O-AS) and phosphorothioate (S-AS) types of oligonucleotides. M-AS **inhibited** translation in vitro (rabbit reticulocyte lysate) of target mRNA at concns. as low as 200 nM (e.g. percent **inhibition** by M-AS 2 at 0.2, 1.0, and 2.0 .mu.M was 40.9 .+-. 5.3%, 50.2 .+-. 4.6%, and 57.7 .+-. 3.6%, resp., n = 4, p .ltoreq. 0.002 vs. control). Similarly, M-AS 2 effectively, albeit partially, **inhibited** **TNF**-.alpha. prodn. by LPS-stimulated macrophages (RAW 264.7 cells). Incubation of cells with 0.5 .mu.M M-AS 2 resulted in 32.6 .+-. 2.6% (n = 3, p = 0.002 vs. control) decrease in **TNF**-.alpha. release. In contrast, S-AS **inhibited** translation of the target mRNA in the rabbit reticulocyte lysate assay, but not in the cell-based assay. In fact, S-AS nonspecifically augmented **TNF**-.alpha. release. O-AS were without effect in either system. Uptake studies with fluorescent M-AS revealed that **inhibitory** effects were seen despite relatively low cellular uptake (intracellular concn. 30.5 .+-. 6.7 nM; efficiency of uptake 0.1%). In contrast, flow cytometric and confocal anal. revealed that S-AS were avidly taken up by RAW 264.7 cells, confirming that their lack of efficacy was not due to lack of uptake. With improved methods of delivery, M-AS may represent an important therapeutic modality.

L8 ANSWER 12 OF 16 CA COPYRIGHT 2002 ACS

AN 125:272478 CA

TI Local administration of **antisense** phosphorothioate oligonucleotides to the p65 subunit of NF-.kappa.B abrogates established experimental colitis in mice

AU Neurath, Markus F.; Pettersson, Sven; Meyer zum Bueschenfelde, Karl-Hermann; Strober, Warren

CS Lab. Immunology, I. Medical Clinic, Univ. Mainz, Mainz, 55101, Germany

SO Nat. Med. (N. Y.) (1996), 2(9), 998-1004
CODEN: NAMEFI; ISSN: 1078-8956

DT Journal

LA English

AB Chronic intestinal **inflammation** induced by 2,4,6-trinitrobenzene sulfonic acid (TNBS) is characterized by a transmural granulomatous colitis that mimics some characteristics of human Crohn's disease. Here, we show that the transcription factor NF-.kappa.B p65 was strongly activated in TNBS-induced colitis and in colitis of interleukin-10-deficient mice. Local administration of p65 **antisense** phosphorothioate oligonucleotides abrogated clin. and histol. signs of colitis and was more effective in treating TNBS-induced colitis than single or daily administration of glucocorticoids. The data provide direct evidence for the central importance of p65 in chronic intestinal **inflammation** and suggest a potential therapeutic utility of p65 **antisense** oligonucleotides as a novel mol. approach for the treatment of patients with Crohn's disease.

L8 ANSWER 13 OF 16 CA COPYRIGHT 2002 ACS
AN 129:310583 CA
TI Therapeutic application of **antisense** oligodeoxynucleotides to **inflammation**
AU Kitajima, Isao
CS Dep. Lab. Med., Fac. Med., Univ. Kagoshima, Kagoshima City, Kagoshima, 890, Japan
SO Approach Dis.: Immunol. Hematol. Cancer, Proc. Fukuoka Int. Symp. Med. Sci., 1st (1996), Meeting Date 1995, 114-127. Editor(s): Niho, Yoshiyuki. Publisher: Kyushu University Press, Fukuoka, Japan.
CODEN: 66OZAP
DT Conference
LA English
AB Lipopolysaccharide (LPS) induced septic shock is assocd. with activation of nuclear factor .kappa.B (NF-.kappa.B). We examd. whether **inhibition** of NF-.kappa.B was protective against LPS induced septic shock in mice. All mice treated with LPS ultimately died within 48 h, while mice pretreated with **antisense** NF-.kappa.B had a significantly better outcome and the survival rate was 60%. Mice pretreated with N-acetylcysteine (NAC) showed nearly 30% protection from LPS induced lethality. Serum IL-6 levels rapidly rose from 113 pg/mL to 577 pg/mL at 4 h after injection in mice pretreated with **antisense** NF-.kappa.B. IL-6, **TNF** and MHC class I mRNA expression were highly induced by LPS in liver and kidneys. Pretreatment with **antisense** NF-.kappa.B caused a profound decrease in both LPS induced IL-6 and **TNF** mRNA. The greatest advantage of **antisense** NF-.kappa.B therapy over the use of NAC is the possibility to suppress NF-.kappa.B strongly for a long term. These findings suggest that the **antisense inhibition** of NF-.kappa.B provides an important new therapeutic approach for **inflammatory** diseases of the liver and kidneys.

L8 ANSWER 14 OF 16 CA COPYRIGHT 2002 ACS
AN 123:167628 CA
TI A member of the NGF/**TNF** receptor induced by lymphocyte activation in **inflammatory** response
IN Lotz, Martin; Schwarz, Herbert
PA Regents of the University of California, USA
SO Can. Pat. Appl., 90 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2108401	AA	19950328	CA 1993-2108401	19931014
PRAI	US 1993-127693		19930927		

AB A receptor (ILA) from lymphoid cells that is activated with proinflammatory agents and a cDNA encoding it are described. The receptor and the cDNA are potentially useful in the diagnosis and treatment of **inflammatory** disease. The transcript was detected by PCR using primers for use in the detection of genes for cell surface receptors in lymphocytes that had been infected with HTLV-1 and activated with PHA/PMA. The transcript was not found in resting cells but was found in cells that had been stimulated with mitogens (PMA, PHA), or anti-CD3 antibodies. ILA is also induced in primary chondrocytes by Il-1.beta. and cytokines that cause cartilage degrdn.

L8 ANSWER 15 OF 16 CA COPYRIGHT 2002 ACS
AN 122:178382 CA
TI **Inhibition** of migration **inhibitory** factor in the treatment of diseases involving cytokine-mediated toxicity
IN Bucala, Richard J.; Mitchell, Robert A.; Bernhagen, Jurgen; Calandra,

Thierry F.; Cerami, Anthony
PA Picower Institute for Medical Research, USA
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9426307	A1	19941124	WO 1994-US5433	19940516
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, UA, UZ				
	PW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2163211	AA	19941124	CA 1994-2163211	19940516
	AU 9468345	A1	19941212	AU 1994-68345	19940516
	AU 692159	B2	19980604		
	EP 702566	A1	19960327	EP 1994-916785	19940516
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09500363	T2	19970114	JP 1994-525764	19940516
	US 6030615	A	20000229	US 1995-471546	19950606
	US 6080407	A	20000627	US 1995-471586	19950606
PRAI	US 1993-63399	A	19930517		
	US 1994-243342	A2	19940516		
	WO 1994-US5433	W	19940516		
	US 1995-462350	A3	19950605		

AB This invention relates to compns. and methods for **inhibiting** the release and/or biol. activity of migration **inhibitory** factor (MIF). In particular, such compns. and methods can be used for the treatment of conditions involving cytokine-mediated toxicity, which include, but are not limited to shock, **inflammation**, graft vs. host diseases, and/or autoimmune diseases. The compns. and methods include agents capable of **inhibiting** MIF biol. activity, MIF receptor biol. activity, MIF gene expression, MIF receptor gene expression, or MIF release in combination with anti-**tumor necrosis factor**-.alpha., anti-interleukin-1, anti-interferon-.gamma., interleukin-1 receptor antagonist, a steroid, a glucocorticoid, or interleukin-10. Such agents can include antibodies, sol. MIF receptor, inactive MIF analogs, small org. mols., oligonucleotides **antisense** to MIF mRNA or **ribozymes** specific for the mRNA, triple-helix forming oligonucleotides, etc. MIF cDNA was isolated and sequenced from a murine anterior pituitary cell line and the human Jurkat cell sequence was cor. The structure, bioactivities, and tissue distribution of MIF were characterized, and MIF was shown to be expressed by both macrophages and pituitary cells. Two forms of the MIF receptor (52-kDa and 72-kDa) were isolated from murine RAW cells.

L8 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
AN 116:75861 CA
TI Oligonucleotides **antisense** to the interleukin 1 receptor mRNA block the effects of interleukin 1 in cultured murine and human fibroblasts and in mice
AU Burch, Ronald M.; Mahan, Lawrence C.
CS Nova Pharm. Corp., Baltimore, MD, 21224, USA
SO J. Clin. Invest. (1991), 88(4), 1190-6
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB Phosphodiester and phosphorothioate oligodeoxynucleotides (18 mers) were constructed **antisense** to sequences of the recently cloned murine and human IL-1 receptors. Murine **antisense** oligonucleotides **inhibited** IL-1-stimulated PGE2 synthesis by murine fibroblasts in culture in a time (days) and concn.-dependent (3 .mu.M-30 .mu.M) fashion.

Murine sense oligonucleotide and an oligonucleotide **antisense** to inhuman IL-1 receptor were without effect. Moreover, murine **antisense** oligonucleotides did not affect **tumor necrosis factor**- or bradykinin-stimulated PGE2 synthesis by murine fibroblasts. Similarly, **antisense** oligonucleotides to the human, but not the murine, IL1 receptor **inhibited** IL-1-stimulated PGE2 synthesis by cultured human fibroblasts. The attention of the cellular response to IL-1 caused by the **antisense** oligonucleotides correlated with a loss in cell surface receptors for IL-1, without any change in the no. of bradykinin receptors on these cells. When **antisense** oligonucleotides were encapsulated in liposomes, they blocked completely the appearance of newly synthesized IL-1 receptors and IL-1-stimulated PGE2 synthesis. In mice, s.c. injection with an oligonucleotide **antisense** to the murine IL-1 receptor markedly **inhibited** the infiltration of neutrophils in response to subsequent injection of IL-1. These data suggest that **antisense** oligodeoxynucleotides may share a role in the design of antiinflammatory therapeutics.

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FULL ESTIMATED COST	64.85	65.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.67	-7.67

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